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JULY, 1960 ... DELAWARE HOSPITAL ISSUE

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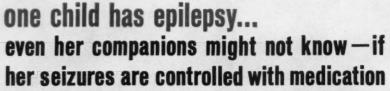
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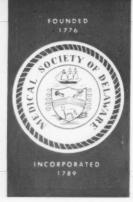
Bibliography: (1) Scott, J. S., & Kellaway, R: M. Clin. North America 42:415 (March) 1958.
(2) Ganoug, L. D., in Green, J. R., & Steelman, H. F.: Epileptic Seizures, Baltimore, Wilkins & Wilkins Company, 1956, pp. 98-102. (3) Bray, P. F.: Pediatrica 23:151, 1959.

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Pelaware Medical gournal

Official Publication of the Medical Society of Delaware

EDITORIAL AND BUSINESS OFFICES
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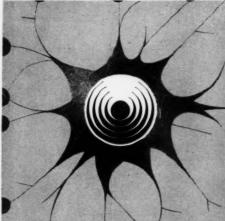


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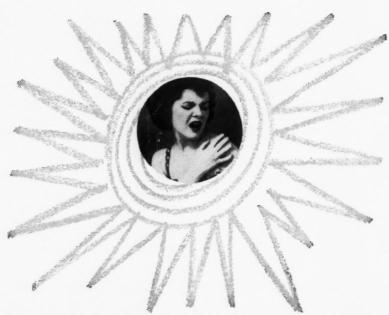


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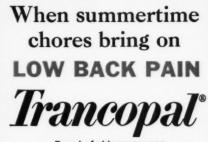
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References: 1. Lichtman, A. L.: Kentucky Acad. Gen. Pract. J. 4:28, Oct., 1958. 2. Lichtman, A. L.: Scientific Exhibit, Internat. Coll. Surgeons, Miami Beach, Fla., Jan. 4-7, 1959. 3. Gruenberg, Friedrich: Current Therap. Res. 2:1, Jan., 1960. 4. Kearney, R. D.: Current Therap. Res. 2:127, April. 1960.

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Projection from Vital Statistics, U.S. Government Dept. HEW, Vol. 48, No. 14, 1958, p. 398.
 Modell, W.: Drugs of Choice 1958-1959, St. Louis, C. V. Mosby Company, 1958, p. 347.



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1. Finland, M.; Hirsch, H. A., and Kunin, C. M.: Read at Seventh Annual Antibiotics Symposium, Washington, D. C., November 5, 1959. 2. Hirsch, H. A.; Kunin, C. M., and Finland, M.: München, med. Wchnschr. To be published. 3. Roberts, M. S.; Seneca, H., and Lattimer, J. K.: Read at Seventh Annual Antibiotics Symposium, Washington, D. C., November 5, 1959. 4. Vineyard, J. P.; Hogan, J., and Sanford, J. P.; Bid.

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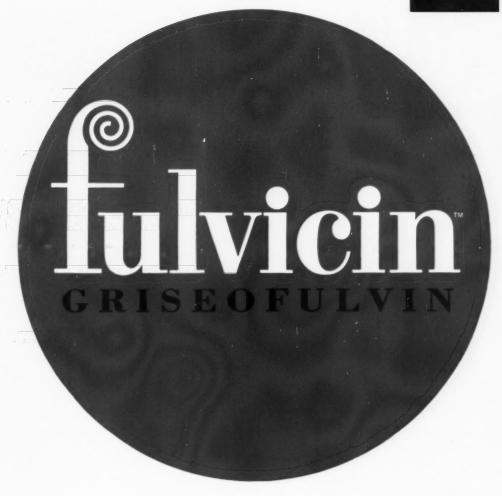
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Delaware Medical gournal

JULY, 1960

NUMBER 7

VOLUME 32

INTERNISTS - QUO VADIS*

REFLECTIONS OF A DIRECTOR OF MEDICINE

LEWIS B. FLINN, M.D.**

Recently Dr. William B. Bean reviewed the progress of Internal Medicine during the past 100 years. Dr. Bean's writings always make delightful reading and this article is no exception. In 1859 life expectancy was 40 years; in 1959 it was 73 years. About 1859 Rudyard Kipling wrote without fear of serious refutation.

"Wonderful little, when all is said, Wonderful little our fathers knew Half their remedies cured you dead Most of their teaching was quite untrue"

In 1959 Dr. Bean concludes that "Internal Medicine can contribute most for the patient where it is learned by hard study and discipline and taught by scholars who have mastered the skills of teaching, the crafts of the clinical arts and the accuracy of laboratory science in the care of the patient."

What can be expected during the next 100 years? If this seems too far to attempt to envision, let us endeavor to look ahead the next ten years. Even this short span may be a little frightening. Let us confine

the query a little more closely. Where is the internist headed in this community in the near future? Let us define an internist in perhaps the simplest terms ever used—as a member of the active staff of the Department of Medicine of this hospital. What path should a younger member of this department pursue?

He should, of course, strive to adhere to the tenets of Dr. Bean's conclusion as stated above. What is truly best for the patient in the long run is always also best for the physician; a fact not always appreciated by medical residents and young practitioners. Nevertheless, the young internist may be in a quandary as how best to proceed or he may be in no quandry at all but erroneously self sufficient!

We have endeavored over the years to develop post-graduate teaching. Could it be that this teaching effort has given the budding internist a false sense of educational security instead of stimulating him to ever greater self educational initiative? Could it be that a sense of smugness has developed that has stifled any smoldering interest in reporting to confreres or preparing for publication interesting cases,

^{*}A copy of this was sent to all active members of the Medical Staff of the Delaware Hospital.

^{**}Director of the Department of Medicine, Delaware Hospital.

clinical observations or clinical investigations? Dr. Paul Tillich is concerned about the loss of what he terms the dimension in depth in the field of religion. Are we in danger of losing what might be called the dimension in depth in the field of medicine? Some of our internists have not completed a three-year medical residency. This should not interfere with their continued growth in Internal Medicine. Even the American Board of Internal Medicine has recognized this and accepts for examination individuals who have been in active practice as long as twelve years. Should a recent graduate of an accredited three-year medical residency strive to become a diplomate of the Board of Internal Medicine? The answer is probably yes, but it should be remembered that although a diploma from the Board is nice, it is not everything. Instead of using the diploma as a stepping stone to other medical interests, some internists consider it an end in itself. Membership in the American College of Physicians or other specialty medical groups is even more to be desired and certainly more stimulating. It is true that a few individuals spend a lot of time going from medical meeting to medical meeting with little real gain except a detailed knowledge of methods of transporta-

tion. On the other hand, the individual who is content to confine his educational pursuits to reading journals in his own arm chair loses perspective and tends to become a medical hermit. One of the most valuable and most important and most rewarding experiences an internist can have is to know personally and be on speaking terms with other internists in other parts of the community, the state, the country, and even throughout the world. Attending medical meetings or visiting other clinics, if done in the right spirit and at reasonably regular intervals, is well worth the time and expense involved.

Let the internist then have a true sense of humility; let him have an awareness that other internists have similar problems for which answers may have been found which can best be learned by personal contact; let the internist have an interest in broadening his medical background. If he will also adhere to the concept of hard study and discipline in the art and science of medicine, he will truly approach fulfillment of his professional capabilities and really excell and exceed his teachers. Should such a course prevail, the story of Internal Medicine in ten, fifty or one hundred years will indeed be interesting to record.

Contributors Column

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PULMONARY SARCOIDOSIS

Pulmonary Function Studies

Sarcoidosis is becoming more important to the clinician as our knowledge of the disease increases. Pulmonary function studies occupy an important position in the evaluation of patients with the pulmonary form of this disease.

JAMES M. HOFFORD, M.D.*

Pulmonary function tests have assumed an important position in diagnosis, followup and evaluation of therapy in various pulmonary disorders. The physiological changes which occur in pulmonary sarcoidosis are to a certain extent typical, but may vary with the stage of progression of the disease.

Three Groups

Three groups of pulmonary function abnormalities have been described in sarcoidosis.¹

In type 1 there is a reduction of all lung volumes with a normal residual volume to total lung capacity ratio. The index of intrapulmonary mixing is normal. The maximum breathing capacity is normal or slightly reduced. There is mild hyperventilation at rest and on recovery from exercise. The blood oxygen saturation is normal at rest and normal or slightly reduced after exercise. The diffusing capacity for oxygen is normal. The ventilation-perfusion relations are normal. There is mild pulmonary arterial hypertension.

In type 2 there is a reduction of lung volumes associated with disturbances in alveolar capillary gas exchange characteristic of the alveolar capillary block syndrome. The residual volume to total lung capacity ratio and index of intrapulmonary mixing are normal. The maximum breathing capacity is well maintained. There is marked hyperventilation at rest and during exercise. The blood oxygen saturation is normal or slightly reduced at rest with a considerable degree of oxygen unsaturation on exercise. There are variable disturbances in ventilation perfusion relationships. There is pulmonary hypertension.

The alveolar capillary block syndrome is characterized clinically by a chest x-ray which shows a diffuse nodular infiltration throughout both lung fields, dyspnea which becomes extreme on exertion, absence of airway obstruction, high maximum breathing capacity, reduced vital capacity and cyanosis not present at rest, but which develops after one minute of exercise. There is a low diffusing capacity for oxygen.

In type 3 the lung volumes are consistent with chronic pulmonary emphysema. There are significant disturbances in ven-

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tilation-perfusion relations and in the oxygen diffusing capacity of the lungs.

In 1952 Riley and Hill² described three cases of sarcoidosis. They were unable to demonstrate any airway obstruction. They pointed out that the vital capacity is a consistent and sensitive guide to the progress of the pulmonary manifestations in sarcoid. The maximum breathing capacity parallels the vital capacity. The three cases presented had been treated with ACTH. The pulmonary function findings were given before and after treatment. They found that the maximal diffusing capacity was strikingly reduced and there was little change following ACTH treatment. The distribution of ventilation and circulation as indicated by the ratio of venous admixture to total blood flow was seriously impaired and response to treatment with ACTH was only moderately striking. The vital capacity, maximum breathing capacity, arterial Po2 and chest x-ray all showed consistent and favorable changes after treatment with ACTH. In these three cases there was relapse after cessation of ACTH. They thought, since the maximal diffusing capacity changes little after ACTH therapy while the x-ray shows a striking decrease in infiltration, that the functional damage to the diffusing surface is irreversible and not affected by a change in the size of the sarcoid nodules. sarcoid nodule apparently destroys alveolar capillaries which do not regenerate when the nodule shrinks. The changes in pulmonary function which result from steroid therapy are apparently related to the degree of resolution of the granulomas and to the extent of the resulting fibrosis. The arterial Po2 must be interperted in terms of overall functional integrity rather than specific physiological factors. The arterial Po2 is a resultant of numerous factors such as ventilation, distribution, diffusion and circulation.

Treatment With Cortisone And ACTH

Stone et al³ described three groups of cases treated with cortisone and ACTH. The one group, consisting of nine cases,

included patients with recent onset of acute symptoms. In this group the vital capacity and total lung capacity were significantly reduced in eight cases. The residual volume was normal or low. There was no emphysema. There was no bronchial obstruction except one case with bronchial involvement. The maximum breathing capacity showed no constant trend. There was hyperventilation at rest, no exercise and no recovery. In five cases there was impaired gas exchange. Four had a slight decrease in oxygen saturation with exer-One had marked unsaturation at rest and with exercise due to an associaated alveolar capillary block. In this group two cases were restored to normal. There was partial improvement in one and most became functionally worse following treatment. They thought that cortisone accelerated the development of pulmonary fibrosis. They suggested that patients with pre-existing evidence of fibrosis, such as reduced lung volumes, do not benefit from cortisone treatment.

Similar To Spontaneous Healing

Siltzbach⁴ has shown that after treatment with ACTH or cortisone the changes are similar to spontaneous healing in a sarcoid lesion. He suggested that we must consider the pulmonary function studies in sarcoid or one can be seriously misled by x-ray changes. Steroid treatment produces initial clearing about the end of the second week of treatment, and it becomes maximal by the end of the fifth week. Cough disappears between the third and fourteenth days. Dyspnea is relieved by the third day. Dyspnea on exertion is relieved within one to twenty one days. Following treatment there was no recurrance of dyspnea in six patients observed three to seventeen months.5 There is clearing in 64% of cases treated with ACTH or cortisone and in 44% of untreated cases.6

In Carr and Gages⁷ series of 194 cases of sarcoidosis of all types, the survival rate for five years was 92% and for 10 years 80%. These are close to the survival rates of normal persons. There were 17

deaths in this series only three of which were due to progressive sarcoidosis and one death was from tuberculosis.

METHODS

The lung volumes, namely vital capacity, expiratory reserve, maximum breathing capacity and maximum expiratory flow rate, were recorded on the 13½ liter Collins spirometer. The spirometer has two motors, one of which turns the drum at a rate of 32 mm in 12 seconds. The lung volumes are measured with this speed. The fast motor turns the drum at a rate of 32 mm per second and the maximum expiratory flow rate is measured while the patient is expiring and the drum is rotating at this rate of speed.

The bronchodilator is Isuprel (1:200) and 1 c.c. is vaporized with continuous oxygen flow into a plastic chamber from which the patient breathes through a one way valve so that he constantly inspires from the chamber and expires into the atmosphere. The oxygen flow is 2.5 liters/minute. Blood pressure and pulse rate are recorded before and after the administration of the bronchodilator.

The walking ventilation is determined by having the patient walk in the clinic hallway at a rate of 180 feet per minute and breathing from the atmosphere through a one way valve into a meteorlogical ballon. The expired air is collected and the volume measured in the Tissot gasometer. The patient walks 4 minutes. The first minute is a warm up period. During the second, third and fourth minutes the expired air is collected and then divided by 3 to obtain the minute walking ventilation. The patient's estimation of dyspnea after walking 4 minutes is recorded.

The residual volume is determined by the open circuit method with the patient inspiring from a continuous source of oxygen and expiring into the Tissot gasometer through a one way valve. After seven minutes of oxygen breathing, the connection to the Tissot is closed and a sample of alveolar air is immediately obtained.

This sample of alveolar air is analyzed for nitrogen and the percent obtained represents the index of intrapulmonary mixing. The residual volume determination is performed three times and an average of the three values is reported. The results should agree within 200 c.c.

Rest And Exercise Tests

Rest and exercise tests are performed as follows: a Cournand needle is inserted into the brachial artery of the left arm. The patient sits in a chair and breathes room air through a one way valve so that the expired air is again collected in the Tissot gasometer. The resting ventilation is recorded for 3 minutes. During the second minute the resting arterial blood sample is taken. This sample is analyzed for oxygen, carbon dioxide and nitrogen content in a Scholander micro gas analyzer. The patient stands and performs an exercise for one minute. This consists of stepping up and back on a hospital foot stool at the rate of 30 steps per minute. During this exercise the patient's expired air is collected in a Douglass bag. Immediately at the end of the exercise the patient sits, the recovery air is collected in the Tissot and a sample of blood is taken. This blood is again analyzed. The exercise gases are analyzed as described under rest. The patient then breathes from a continuous supply of oxygen through a one way valve for 15 minutes. An arterial blood sample is again taken and analyzed as before.

ABBREVIATIONS

V.C.—vital capacity

M.E.F.R.—maximum expiratory flow

T.L.C.—total lung capacity

R.V.-residual volume

P.—predicted value

B.—before bronchodilator

A .- after bronchodilator

O.—observed value

R.Q.—respiratory quotient

I.I.P.M.—index of intrapulmonary mixing

CHA	RT 1				CLINICAL SU CASES OF SARC			
CASE	RACE	SEX	AGE	DURATION DISEASE (YEARS)	RADIOLOGIC FEATURES	RESPIRATORY SYMPTOMS	PERIOD OF TREATMENT (YEARS)	RESPONSE TO TREATMENT
1.	С	F	37	8	1951 - Bilateral hilar node and lung infiltration. 1954 - Tenting of diaphragm. 1959 - Fibrotic replacement and apical retraction.	1952 - Cough, dyspnea on exertion. 1955 - Dyspnea at rest. 1956 - URI. 1959 - Allergic rhinitis.	4	Metecorten 7-55 to 7-59. Well by May 1956. Now has slight cough.
2.	С	F	34	2	1957 - Bilateral lung mottling. 1958 - Clearing with residual fibrotic change.	1957 - Exertional dyspnea. 1959 - None.	1	Metecorten 9-57 to 7-58. Maximal improvement 10-57.
3.	W	М	34	4	1956 - Bilateral flocculent densities	1955 - None 1959 - None	1/6	Asymptomatic. Metecorten 2 mos. 1956 associated with x-ray clearing.
6.	С	М	55	2	1957 - Right hilar enlargement with soft tissue extension. 1959 - Decrease right hilar density.	1957 - Right side pneumonia. 1959 - None	0	Asymptomatic.

Seven patients with suspected sarcoidosis have been followed in the Delaware Hospital Pulmonary Function Loboratory for periods ranging up to three years. Four patients (1, 2, 3, 4) have been shown to have sarcoidosis by lymph node or lung biopsy.

CASE	RACE SEX AGE KNOWN DURATION DISEASE (YEARS)		RADIOLOGIC FEATURES	RESPIRATORY SYMPTOMS	PERIOD OF TREATMENT (YEARS)	RESPONSE TO TREATMENT		
5.	С	F	38	1/2	1959 Prominent hilar areas, diffuse haziness, increased broncho-vascular markings.	1959 Cough, tightness in chest.	0	
5.	С	М	69	4	1955 Left lung has a mottled density with a right middle lobe density. 1959 No change.	1955 Dyspnea on exertion, choking sensation. 1959 Dyspnea, substernal crushing pain.	0	1955 Congestive failure. 1959 Acute pulmonary edema
7.	С	М	48	3	1957 Bilateral hilar lymph node enlargement. 1958 Same.	1956 Cough and fever. 1959 Cough.	0	Less cough after excision of tracheal polyps.

Two cases (6, 7) have inconclusive biopsies with clinical conditions suggesting sarcoid. One case (5) had a positive lung biopsy for sarcoid, but eventually developed a positive culture for tuberculosis from the lung tissue obtained at biopsy.

CASE	TIME OF STUDY		V.C. (CC)		:	SEC V.C.			SEC.	•	T.L.C.		R.V. (CC)		R.V. %	
		P.	В.	Α.	P.	В.	A.	P.	В.	A.	P.	0.	P.	0.	P.	0.
1	3-58	2960	1840		90	100										
	2-59	2940	1180		90	100		4-6	3.2							
	2-59										4250	2321	1310	1141	31	49
2	7-57	2949	1450	1589	90	100	100									
	11-57	2949	1770	1770	90	95	98									
	1-58	2940	1950		90	100										
	8-58	2910	2190		90	100										
	7-59	2930	2320		90			4-6	4.1		-					
	6-59										4060	3704	1130	1384	28	37
3	4-57	4331	5222		90	100										
	2-59	4410	5480		90	99		1:-6	6.4							
	2-59										6650	6501	2240	1021	34	16
6	6-57	3666	2494	2140	90	84	94									
	12-58										5420	3993	1760	1499	33	38
	7-59	3630	3240	3060				-6	4.6	5.3						
5	7-59	2845	935	1150				4-6	2.3	2.7						
	7-59										3960	1890	1115	955	28	50
5	5-59	3380	3250	2950				4-6	3.2	3.6						
	5-59										5600 -	5537	2220	2287	39	41
7	7-57	3691	2753	3717	90	76	76									
	5-58	3691	3555		90	73										
	8-58	3691	3350		90	73										
	11-58										5200	5462	1270	2630	24	48
	7-58	3650	3250	3300				4-6	1.8	2.0						

CHART 3

Three patients (1, 2, 3) were treated with meticorten for periods varying from 1/6 to 4 years. The patient (1) treated for 4 years has shown the most damage as seen by x-ray progression of fibrosis and decreasing lung volumes on pulmonary function tests. (see Charts 3 and 4).

				VEN	TILAT	ION				
CASE	TIME OF STUDY	M.B.C.(L.)			M ² OF AIR FOR WALKING	WALKING INDEX NORMAL BELOW	SUBJEC- TIVE WALKING DYSPNEA	TIDAL AIR (C.C.)	EFFECTIVE PHYSIO- LOGICAL QEAD	D.S. T.A. (%)
		PRED.	BEFORE	AFTER		0.25			SPACE (C.C.)	
1	3-13-58	91	94							
	2-4-59	90	63		10.5	0.27	NONE			
,	4-22-59							270	146	54
2	7-10-57	94	89	87	5.5	0.1	3+			
	11-5-57	95	85	90	7.6	0.13	NONE			
	1-23-58	94	74		6.9	0.12	NONE			
	8-19-58	94	101		8.7	0.14	NONE			
	7-14-59	92	99		8.0	0.15	NONE	413		
3	4-18-57	140	182							
	2-3-59	138	147		9.0	0.12	NONE			
	4-1-59							830	213	26
4	6-25-57	98	75	103	4.2	0.09	1+			
	7-16-59	101	100	116	7.8	0.13	NONE	465		
5	7-22-59	87	44	42	15.9	0.59	2+			
	7-21-59							285	146	51
6	5-5-59	87	67	69	12.9	0.33	2+			
	6-9-59							632	322	51
7	7-5-57	108	87	80	4.5	0.09	1+			
	5-15-58	108	78		7.6	0.17	1+			
1	8-5-58	84	71		8.2	0.20	1+			
	7-15-59	105	57	62	10.1	0.32	NONE	389		

CHART 4

Two patients (2, 3) were treated 1.0 year and 1/6 year respectively with meticorten. They have shown improvement in pulmonary function tests. The x-rays have shown clearing of the lung mottling and flocculent densities with residual fibrotic change. Patient No. 4 did not receive

meticorten and has shown considerable improvement. (Chart 4)

The four cases of proven sarcoidosis show evidence of a restrictive type of lung disease with a considerably reduced vital capacity and a slightly reduced maximum

CASE	TIME OF STUDY	RESP. RATE		CO ₂ OUTPUT CC/MIN/M ²		KE In/ m ²	R.	Q.	VENTIL L/M		ALVEOLAR VENTILATION L/M ²	IIPM
		REST	REST	EX.	REST	EX.	REST	EX.	REST	EX.	REST	_
1	4-59	28	95		118		0.8		4.7	11	1.6	1.29
2 7-	7-59	24	130	243	128	339	1.02	0.72	6.0	7.9		
	6-59											1.25
3	2-59											1.69
	4-59	13	159	381	164	528	0.97	0.72	5.9	10	3.96	
4	12-58											1.45
	7-59	18	128	323	159	502	0.8	0.64	4.7	9.7		
5	7-59											1.04
	7-59	37	115	265	143	353	0.80	0.75	6.5	15.9	2.97	
6	5-59											1.75
	6-59	15	120		152		0.79		5.5		2.70	
7	11-58											3.28
	7-59	21	125	273	141	376	0.88	0.72	4.76	10.7		

CHART 5

breathing capacity. The maximum expiratory flow rate and the three second vital capacity are normal. The total lung capacity is reduced. The residual volume is normal. The residual volume to total lung capacity ratio is relatively normal.

Patient No. 5 has evidence of a restrictive and an obstructive type of disease with a maximum expiratory flow rate of 2.3 liters/second and a low maximum breathing capacity.

Patient No. 6 has mild bronchospasm with a maximum expiratory flow rate of 3.2 liters per second and a maximum breathing capacity of 67 liters per minute.

Patient No. 7 has findings which suggest the development of early emphysema. The residual volume is twice normal and the index of intrapulmonary mixing is quite high, indicating uneven distribution of gases within the lungs.

Patients 1, 5, and 6 all hyperventilate on walking as judged by the L./MIN./M² of air used to walk. It is interesting that patient No. 2 demonstrated improvement in vital capacity and maximum breathing capacity but increased the walking ventilation from 5.5 to 8.0 L./MIN./M² which suggests that other factors are tending to increase the work of breathing. The same trend occurred in patient No. 4.

The walking index is the number of liters of air used per minute in walking divided by the maximum breathing capacity and represents the per cent of the maximum breathing capacity used in walking. When subtracted from 100 we have the

CASE	TIME OF STUDY		GEN SAT				CO2 CO VOL.	nten t %	P _{co2}	PH		
		PRED. REST	REST	EX.	02	PRED.	REST	EX.	02	PRED.	REST	REST
1	4-59	96	92	77		49	49	48		40	37	7.45
2	1-58	96	90	75		49	47	45	46	40		
3	4-59	96	96	91		49	50	50		40	35	7.50
Ĺ;	1-59	96	92	88	100+	49	50.4	50.3	49.8	40	36	7.48
5	7-59	96	92	81		49	39	38		40	30	7.45
6	6-59	96	85		100+	49	47			40	39	7.40
7	5-58	96	80	81		49	44	44.9	45	40		

CHART 6

breathing reserve while walking. Normally the walking index is less than 0.25 or 25%.

All the patients were hyperventilating at rest (Chart 5). The resting ventilation should be 3.5 L./MIN./M².

The alveolar ventilation is normally 2.3 L./MIN./M². Patient No. 1 has a somewhat reduced value.

The respiratory rates are rapid.

The respiratory quotient (R.Q.) represents the carbon dioxide output divided by the oxygen consumption. The R.Q. is normally 0.8.

The increases in oxygen consumption on exercise in these patients indicate that the amount of exercise is sufficient. Since the amount of exercise has been uniform as judged by the oxygen consumption, we are able to compare the other values obtained on exercise from different patients and from the same patient at different times.

The measurements of oxygen saturation at rest and on exercise are similar in the four cases of sarcoidosis (Chart 6). They are all above 90% at rest. The marked drop in oxygen saturation on exercise suggests the presence of an alveolar capillary block. The drop from 96% to 91% in O.M. is the one test indicating the presence of an abnormality.

Patients No. 6 and 7 have very low oxygen saturations at rest which makes one think of other diseases than sarcoidosis.

Certainly they are not typical of the other cases of sarcoid in our series.

The Pco2 in mm Hg demonstrates the absence of carbon dioxide retention in these cases

SUMMARY

- 1. The typical pattern of pulmonary function tests in pulmonary sarcoidosis is
- 2. The influence of ACTH and cortisone on pulmonary sarcoidosis and accompanying pulmonary function tests is reviewed.
- 3. Seven cases of suspected pulmonary carcoidosis are presented with emphasis on the pulmonary function tests. The four proven cases of sarcoidosis presented here display a pattern of pulmonary function compatible with other presentations in the literature.
- 4. The remaining three cases deviate from the typical pattern of sarcoidosis. The pulmonary function tests in these three cases present variations which make one question the validity of the diagnosis of sarcoidosis.
- 5. Serial pulmonary function tests present a quantative measure of the progress of the disease and effect of therapy.

6. The effect of steroid therapy is discussed. Long term therapy may be harmful in this disease.

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Contributors Column

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MEATAL STENOSIS

AN EASILY DIAGNOSED BUT FREQUENTLY MISSED UROLOGIC DISEASE IN CHILDREN

• Urethral meatal stenosis is a relatively simple condition that can be cured by a simple surgical procedure. As is true in so many conditions, it must be considered as a possibility if the diagnosis and successful treatment is to be accomplished.

L. WILLIAM FERRIS, M.D.*

Urethral meatal stenosis in male children and adults is a frequently overlooked and easily treated urologic lesion with serious aftermath, if allowed to persist untreated. Although all obstructive lesions of the genitourinary tract are important, there is none more easily diagnosed or treated than urethral meatal stenosis in the male. A similar lesion occurs in the female; however, it is less easily diagnosed and treated.

All genitourinary lower tract obstructive lesions lead inevitably to the same pathologic consequences, and they share the same symptomatology. The increased hydrostatic pressure proximal to the area of obstruction causes dilation and thinning of the urethra which, if severe, may progress to the formation of diverticuli with subsequent rupture and extravasation of urine.

The bladder responds to the stress of obstruction initially by hypertrophy. As its capacity for hypertrophy is reached, di-

latation occurs, and eventually the point is reached where its contractile power is impaired. It is unable to empty completely, and residual urine with stasis and infection is the result.

The upper urinary tract is not involved early as a rule, but with progressively severe obstruction the physiologic "ureterovesical valve" becomes forced open, allowing transmission of increased pressure and reflux of infected urine up the ureter. This increased pressure may be transmitted to the kidney itself with the development of a hydronephrosis and pyelonephritis, and resultant permanent damage to the renal parenchyma.

Enuresis Complaint Misleading

Fortunately, most patients with meatal stenosis are seen before the stage of hydronephrosis is reached. Unfortunately, however, many have existed for years before diagnosis is made. This situation appears to be due to the fact that a careful history

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Figure 1



Figure 2 (oblique)



Figure 3

is not taken, and infection does not occur until late in the course of the disease. Many of these children have been seen at least once for the chief complaint of enuresis before the diagnosis is finally made. Because the urinalysis is normal, these children are frequently labeled emotional bedwetters.

The parents have often noted only the presence of bedwetting, which is impressive and annoying because of the wet bedclothes, and this completely overshadows the other symptoms. These must be brought out by direct questioning, as a rule. Since the urinalysis is normal until late in the progression of these obstructive lesions, the history is all-important in early diagnosis. These symptoms are common to all lower urinary tract obstructive lesions, and are much more reliable than laboratory data.

Frequency during the daytime is usually marked. Often the child voids every two or three hours, but in most cases over six times a day. Enuresis and waking at night

to void are persistent with one or several episodes during the night. These symptoms persist in spite of withholding fluids.

Urgency is often present, but not necessarily so.

Obvious straining, with or without a narrow stream, is common.

Interrupted stream is an early sign of bladder decompensation. This occurs when the stream is stopped for a few seconds durthe act of micturition. This interruption represents bladder rest.

Double voiding is a rather late symptom which usually follows interrupted stream in its appearance, i.e., the child, after voiding is over, must void again a few minutes later. This represents residual urine which he is able to void only after the bladder rests.

Dysuria is not frequently noted until the infected stage is reached.

Suprapubic pain may or may not be present, and it is not a reliable sign.

These symptoms are the same for any obstructive lesion in adults or children, and should lead to the investigation of the lower urinary tract in all cases where they exist.

Meatal stenosis is one of the commonest of these lesions, and all that is needed for diagnosis is examination. The meatal dimple is frequently normal in appearance; however, the actual lumen, upon spreading the meatus, is pinpoint in size, and is obviously small. The importance of spreading the meatal dimple cannot be over emphasized, as the dimple is usually normal in appearance, but the actual lumen of the terminal end of the urethra may be narrow. The inspection of the meatus should be a part of every routine physical examination in the male, whether symptoms are present or not.

Treatment Simple

The treatment of these lesions is simple, and can be done wherever the equipment for repair of minor laceration is available. The glans is first prepared by washing with pHisohex and water, and draped with a sterile sheet. A small amount of anesthetic jelly is then introduced about onehalf centimeter into the urethra. After a few minutes, a local anesthetic can be introduced through the urethra into the periurethral tissues with a #24 or #25 needle; ½ cc. is usually enough. A scalpel blade is then inserted into the urethra and drawn ventrally, creating a slit continuous with the urethra, enlarging it in a ventral direction. (Figs. 1 and 2). The urethra and epithelium of the glans are then approximated to cover the denuded surface with three or four plain catgut sutures of #0000 or #00000. (Fig. 3). This prevents healing across of the meatotomy incision. parents should be instructed to spread the incision daily and to give the child warm baths twice daily for comfort and local hygiene. No dressing, salves or ointments are applied. The child should be seen in four to seven days to check the meatus, since if healing has begun, at this point the incision can be dilated and separated without difficulty.

Relief of symptoms is usually dramatic and apparent in from five to seven days. Of course if symptoms are not relieved in a week or two, complete urologic examinations should be done. It does not appear to be necessary to investigate further if meatotomy results in a normal voiding pattern and sterile urine.

In the last two months, sixteen male children have been seen and treated in the Urology Clinic at the Delaware Hospital for urethral meatal stenosis. None of these children had infection, and all were referred because of bedwetting or daytime frequency by their local doctors, the parents themselves, or by the school nurse, who found that the extreme daytime frequency was interfering with school work. In these sixteen cases there was one recurrence which was felt to be due to the parents' failure to spread the incision daily. This was corrected at the seventh day followup visit.

Condition Often Familial

This lesion is often familial, and questioning the parents may reveal siblings with the same symptoms to a greater or lesser degree. It is felt that regardless of symptoms, where this lesion occurs in one child, all male siblings should be examined. The following case report illustrates rather dramatically the results of such routine questioning at examination.

CASE REPORT

The patient, a five year old boy, was referred to the Urology Clinic from the Pediatric Clinic with the following history:

Chief complaint was that of frequency of urination. He was bladder trained at the age of two, and had had normal bowel training with control complete at the age of two, according to the mother. From that time on the parents had noted frequency, which occurred about every forty-five minutes. He had always wet the bed at night. The symptoms had remained stable and had persisted with about the same amount of frequency until he was seen in Urology Clinic. Additional symp-

toms which had been noted, but which were learned only as a result of direct questioning, were urgency, interrupted stream, and double voiding, since about the age of three. There was no history of urinary tract infection, or of suprapubic pain. In spite of the fact that the parents awakened the child during the night, the child persisted in wetting the bed. Water restriction after 6:00 P.M. was tried, but this also met with failure, forcing the parents to seek medical attention. On questioning the mother about siblings, there were three brothers, all of whom had the same problem of enuresis and daytime frequency. The father and mother had a normal voiding pattern.

The past history was negative. The physical examination was unremarkable except for a very tight meatal stenosis, which was obvious on examination after spreading the meatal dimple. Blood urea nitrogen and urinalysis were normal; the urine culture was sterile. Cystoscopy was performed on this child because of the long duration of symptoms and the history of double voiding; moderate trabeculation was found as the only abnormality. There were no congenital valves or ureteroceles noted; there was no urethral stricture above the meatus.

Meatotomy was performed in the previously described manner, and the child was given an appointment to return in one week. The mother was instructed to spread the meatus daily, and to give the child two hot baths daily. When the child returned in a week, the meatus was found to be adherent across the meatotomy incision, due to the mother's failure to separate the incision daily. For this reason, the child was seen again in three days, the meatus again dilated. Ten days following meatotomy the voiding pattern revealed no nocturia or enuresis, in spite of the absence of restriction of fluid intake at night, and the daytime frequency was not more than four to five times daily. There was no interrupted stream, and double voiding had ceased.

Similar Lesions In Siblings

The eight year old sibling was examined, and the history revealed enuresis of approximately six to eight months' duration, with daytime frequency of approximately every half to three-quarters of an hour, which had begun within the last year and and a half. The urinalysis report was negative for albumin, white cells or red cells, and the culture was sterile. The physical examination revealed a lesion identical to the first case, with a very narrow urethral meatus. This was corrected by meatotomy under local anesthesia, without cystoscopy. On followup visit one week later, there was marked improvement, with no enuresis, a normal voiding pattern of from four to six times daily, and with no double voiding or straining.

The third boy in this family was examined at the age of four years. He had had daytime frequency or every fifteen minutes to every half hour, with straining, interrupted stream; bedwetting had occurred every night since the stage of bladder training. Meatotomy was done under local anesthesia, and one week following this there was marked improvement, with no enuresis, no double voiding or straining, and a daytime frequency of from three to five times.

The fourth child in this family was five years old, with a similar complaint of enuresis since the stage of bladder training, and daytime frequency of every one to three hours. The physical findings and urinalysis reports were identical to those of the other three siblings, and meatotomy was done under local anesthesia. One week post-operative his symptoms were completely relieved.

Successful Results

These patients have been followed for approximately six weeks, and they all have normal voiding pattern, with no enuresis.

It is difficult to understand how the parents of these children allowed them to go on with symptoms of such a severe degree for so long a time, without seeking

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medical attention. However, all of these children had been seen at various times, and all had been given at least one or two physical examinations without these lesions being observed. There have been numerous other instances illustrating the familial incidence of meatal stricture, with combinations of two siblings, or father and son. Occasionally the father may recognize the same symptoms in the child, when diagnosis is established in himself.

There have been numerous case reports wherein an adult patient presenting with lower urinary tract obstructive diesase identical with that of hypertrophy of the prostate has been found on urologic examination to have hydronephrosis, chronic cystitis, pyelonephritis, and mildly to moderately decompensated kidneys, with bladder trabeculi; the sole urologic lesion on complete genitourinary investigation was found to be meatal stenosis. A careful history of the voiding pattern in the majority of these cases has revealed that these abnormal symptoms have been present for many years, frequently for as long as the patient can remember, and through several physical examinations.

Conclusion

There are few lesions of functional importance that are more easily diagnosed

and treated than urethral meatal stenosis in the male, and none should go unrecognized after physical examination. The results of neglect of meatal stenosis are serious damage to the entire urinary tract, with irreversible damage to the kidneys if allowed to progress in its severe form. The diagnosis is easily made, and the treatment is a simple office procedure, with a very minimal recurrence rate, and with virtually no complications.

It is important to follow these children postoperatively to see that the voiding pattern has become normal, and that any existing urinary tract infection is eradicated. If this has not occurred, a more complete evaluation of the genitourinary system should be done, with cystoscopy and excretory urograms, to aid in the discovery of other lesions such a ureterocele, and anterior or posterior urethral valves. Because of the high familial incidence of meatal stenosis, all siblings should be examined when the lesion is found in one child. The presence of a normal urinalysis report is more common than not in these children, and should not lead to the diagnosis of emotional enuresis.

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HEARD AT THE 1960 A.N.A. CONVENTION

Voicing a protest against what they considered unfair attitudes on the part of the medical profession, delegates to the A.N.A. adopted a legislative report that strongly criticized the American Medical Association and individual physicians for their efforts to alter the American Nurses Association's support of the Forand bill.

"Physicians . . . have implied that nurses cannot make an intelligent decision about a social issue . . . (the A.M.A.) has taken advantage of the close working relationship between members of the two professions and the concept that this relationship is that of master and servant still appears to persist in the thinking and attitudes of many doctors." (Supplemental Report of the Committee on Legislation). R. N., July, 1960.

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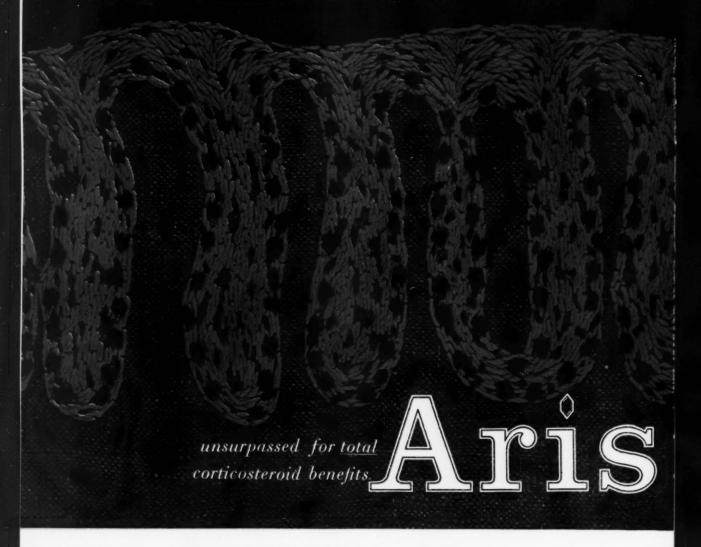


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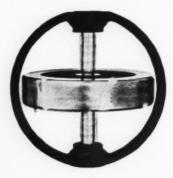
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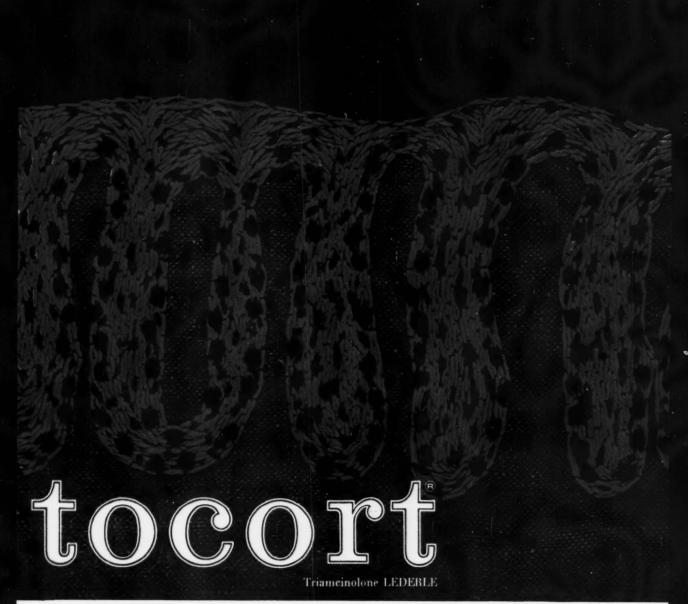


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Kao, K. T.; Leake, D. A.; Bauer, H. G., and Berger, H. E.; Am. J. M. Sc. 236:720 (Dec.) 1958. 18. Council on Drugs: J.A.M.A. 169:257 (January) 1959.



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THE RAT OVARY HYPEREMIA PREGNANCY TEST

A CLINICAL LABORATORY CORRELATION

 The desirability of having a simple but accurate test for pregnancy is obvious. The favorable and unfavorable aspects of the rat ovary hyperemia test are discussed.

*JOHN M. LEVINSON, M.D.

**EDWIN M. RICHARDSON, Ph.D.

Ordinarily the diagnosis of pregnancy offers little or no difficulty and the patient is usually aware of her true condition before she consults the physician. In a small number of cases, however, the diagnosis is not easy despite all the known methods at our command. Confusion may occur particularly in the first few months of pregnancy when the uterus is a pelvic organ, in patients with pelvic tumors, or those with abnormal signs and symptoms. For this reason, as well as to establish an early diagnosis in the apprehensive patient or the patient with a problem of infertility, a reliable laboratory test is needed. For the last four and one-half years the rat ovary hyperemia test for pregnancy has been the method principally employed in the laboratory of the Delaware Hospital. This test is based upon the hyperemic response of the rat ovary to chorionic gonadotrophin in the test serum which is a reflection of early trophoblastic activity in pregnancy. The advantages claimed for this technique are: ease and speed of performance, sensitivity, saving in cost of the test animals, and saving in space required for housing them. A disadvantage is the greater experience required for reading the result. The purpose of this paper is to determine the accuracy of the method in this laboratory by correlating the results with the clinical findings.

Method

One cc. of serum was injected intraperitoneally into each of two immature female rats of Wistar or Holtzman strain, 26-32 days old, weighing 40-60 grams and having the vagina still closed. After 14-20 hours, the rats were killed with ether, and the ovaries examined. If at least two ovaries showed a definite diffuse reddening, the test was reported positive. If only one ovary appeared slightly hyperemic, the test was reported doubtful, and was

^{*}Assistant, Dept. OB-GYN. Delaware Hospital.

TABLE I

Clinical Diagnosis	Number of Tests	Positive ROH	$\frac{Negative}{ROH}$		
Intrauterine pregnancy	52	48 (2 weakly positive)			
Pseudocyesis	2	2	0		
Unruptured ectopic pregnancy	2	2	0		
Ruptured ectopic pregnancy	2	0	2		
Ovarian dysfunction	25	1 weakly positive	24		
Incomplete abortion	5	0	5		
Normal-patient post hydatidiform mole	5	0	5		
Myoma uteri	5	0	5		
Cervical stenosis with amenorrhea	1	0	1		
Ovarian cyst	2	0	2		
Total	101	53	48		

repeated, preferably after waiting a few days.

Material

One hundred and five consecutive rat ovary hyperemia (ROH) tests were performed on ninety-four patients from the private practice of one of the authors, during almost a three year period. Clinical follow-up was not available on four tests, and therefore these were excluded from the analysis. All other tests have been verified by complete follow-up of the patient with definitive clinical diagnoses.

Results And Discussion

The results are shown in Table I.

False Positive Reactions

There were three false positives. One patient had hypomenorrhea with equivocal symptoms of pregnancy and an ROH test was reported as "weakly positive—suggest repeat." An ROH test repeated in 48 hours was negative. The clinical diagnosis was ovarian dysfunction.

The other two cases were of patients with pseudocyesis. One patient with a false positive test was a diabetic, gravida I, para O, with great anxiety about becoming pregnant. She was amenorrheic for $4\frac{1}{2}$ months before resuming normal menstrual function. Most of the early signs and symptoms of pregnancy except uterine enlargement were present.

The other patient was a multigravida with a long and difficult obstetrical history. A positive ROH test was obtained, the patient having amenorrhea and signs and symptoms of pregnancy. Following several weeks of amenorrhea, irregular and heavy bleeding ensued and a D & C was done, disclosing secretory endometrium.

The erroneous test results on the second and third patients were probably due to the prolonged corpus lutem function which occurs in pseudocyesis. In occasional cases such as this, the pregnancy test may be weakly positive, suggesting that there is an excessive production of luteinizing gonadotrophic hormone in this disorder.² Since laboratory tests may give erroneous results, the diagnosis in the case of these patients must be made on the basis of clinical findings.

False Negatives

There were four false negatives. The first patient in this group was approximately 28

days past an expected menstrual period when the false negative ROH test was obtained. A test repeated 4 weeks later was strongly positive and the patient's pregnancy progressed uneventually to term. Two other patients were 7 and 33 days past the expected time of menstrual flow, and had false negative ROH tests. Both of these patients had uneventful pregnancies. The fourth patient in this group had a weak positive test four days after missing an expected menstrual period and a negative test three days later. During the time of testing she had vaginal bleeding and was considered a threatened abortion. This patient is now 7 months pregnant and her course has been uneventful since this occurence.

Avoidable Inaccuracy

The inaccuracy of two of the four tests here might have been avoided by the use of a pituitary synergistic reagent as described by Rakoff.3 This reagent, which has been used to heighten the ovarian hyperemic response particularly when testing patients who are only a few days past an expected menstrual period, has generally increased the accuracy of the test. This is the time when a false negative is most likely to occur. Many authors state that a pregnancy test may be inaccurate in the first two weeks following the missed menstrual period and that a negative result at this time carries little value. Nevertheless one patient only 21/2 days past an expected menstrual flow, had a strongly positive test and carried a pregnancy to term. In addition, two unruptured ectopic pregnancies were reported as positive, one test being done when the patient was only 10 days past an expected menstrual period. Later, one of these ectopic pregnancies ruptured. At this time the test was negative. The other negative ROH test was in a patient with a ruptured ectopic pregnancy and the results agreed with the clinical findings at that time.

Although this test is performed in many laboratories by the injection of urine intraperitoneally, it is considered more accurate

to use serum. This is based on the work of Foote and Jones4 who have found that the level of chorionic gonadotrophin roughly parallels that of the serum. These authors state that in their experience no pregnancy test based upon urinary excretion of chorionic gonadotrophin approaches those based upon blood serum concentration in accuracy or sensitivity.

Reading Of The Test Important

Any biologic test may be subject to a number of errors. Reading the test is one of the possible sources of error. In a good light, a positive test shows a distinct line of demarcation between the uniformly diffuse red of the ovary and the pink of the fimbriated portion of the fallopian tube. The difference of sensitivity in individual rats, probably related to endogenous follicle stimulating hormone (FSH) production is another uncontrolled factor. Fried and Rakoff reported a decrease in the number of false negatives, and a sharpening of the end point of the 2-3 hour urine test by use of the FSH synergist.

The performance of the test by a number of different technicians could have contributed to errors due to inexperience in reading the result, or to injection of animals that were too young, and therefore less sensitive, or too old, with the possibility of a false positive due to endogenous production of luteinizing hormone (LH). Careful attention to these sources of error should improve the accuracy of the test.

Summary

- 1. The results of 105 consecutive ROH pregnancy tests were correlated with the clinical findings. In 101 tests, accurate clinical follow-up was available. Out of these, 94 were correct, showing an accuracy of 93.1%.
- 2. The sources of error of the method in our hands have been discussed.

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• The number of agents formerly recommended for treatment of the Stokes-Adams syndrome is evidence of their general inadequacy. The use of the cardiac pacemaker attached to an internal electrode is the first major breakthrough in the management of this fatal condition.

RECENT ADVANCES IN THE THERAPY OF

R. A. KAHLBAUGH, M.D.*

J. RICHARD DURHAM, M.D.**

The Stokes-Adams syndrome, cerebral ischemia associated with complete heart block and idioventricular rhythm due to asystole or extreme bradycardia, remains a therapeutic problem despite the availability of many therapeutic agents. The sympathomimetic amines have been used most commonly and continue to maintain an important place in the therapeutic regimen. Isopropylarterenol, ephedrine sulfate and epinephrine are many times effective in preventing Stokes-Adams attacks in patients with complete heart block. Bellet1,2 has reported good results, with conversion to normal sinus rhythm, from the use of sodium lactate intravenously. Others have not had similar success with this agent. Recently Friedberg4 has reported successful termination of Stokes-Adams attacks and prevention of further episodes with prednisone or hydrocortisone. Many times steroids had to be continued for prolonged periods,

and in one case at a dosage of 60 mgms. a day.

Not A Common Phenomenon

Dosage dependency, however, is not a common phenomenon in the therapy of this syndrome. Chlorothiazide or hydrochlorothiazide in addition to steroids may be helpful. The action of these latter agents is probably due to reduction of serum potassium levels. Some authors, however, suggest that the anti-inflammatory effect of the steroids is their mechanism of action. Zoll et al5,6,7 have reported extremely good results with the external conventional pacemaker. We have not experienced similar good results in a much smaller number of The muscular contraction of the chest wall and chest pain produced have severely limited its use in our hands. In spite of this varied list of therapeutic agents, none is uniformly effective.

^{*}Resident in Medicine, Delaware Hospital. **Attending Chief, Department of Medicine, Delaware Hospital.

^{*}Atronic Products, Inc., Bala Cynwyd, Pa.

STOKES-ADAMS SYNDROME

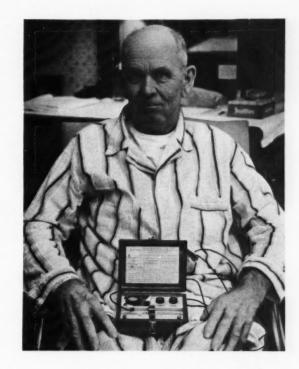


Figure No. 1 — Patient with intracardiac electrode in place connected to the Atronic pacemaker.

Recently Atronic Products, Inc.,* has produced a small portable internal pacemaker which we have had occasion to use in one patient with complete heart block and Stokes-Adams syndrome.

The Atronic Pacemaker

The Atronic pacemaker (Fig. 1) is a compact 51/2"x41/2"x13/4" unit weighing approximately two pounds which supplies extraneous cardiac stimulation by direct application of the electrical stimulus to the myocardium. The current delivered may be set from 0 to 24 milliamperes, and the rate of stimulation can be set between 25 and 120 per minute. The pacemaker operates immediately without requiring time for warming up. It is powered by two batteries which will last an average of six months of continuous use. A galvanometer is present which registers impulse rate when the switch is on "stimulate;" or the impedence to flow of electrical current when the switch is so set. All control knobs are protected by the outer case and cover so that the settings cannot be disturbed accidentally. The patient lead is permanently attached to the unit and is attached to the stimulating electrode and the indifferent electrode by a jack which can be disconnected.

Methods

Methods of introducing the intracardiac electrode.

(A) A flexible, tempered, insulated stainless steel wire is enclosed in a stainless steel tube. This passes through a 16 gauge hypodermic needle through which the wire is pushed into the myocardium. Overpenetration is prevented by a stop on the wire. The needle and tube are retracted over the wire. The intracardiac electrode is negative and has a white marker. The positive elec-

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trode is attached to the skin or imbedded subcutaneously.

More recently a flexible stranded steel wire has been used which may be threaded through a 20 gage spinal needle into the myocardium.

- (B) The wire electrode may be sewn directly into the heart muscle via a small thoracotomy.
- (C) Direct placement of the electrode is also possible via a #6 cardiac catheter inserted through the right jugular vein and placed into the cavity of the right ventricle. (Fig. 2)

Each of these methods has its advantages and disadvantages. Application through a needle transthoracically is easy and can be done quickly in an emergency. Placement in the ventricular wall may be technically difficult, but with the switch on impedence, a sharp decrease in deflection is observed when the electrode is properly placed. The disadvantages of this method are (1) the possibility of the electrode becoming displaced; (2) the possibility of infection; (3) the possibility of hemorrhage; and (4) the inevitable fibrosis about the electrode resulting in loss of capture.

Direct Placement

The direct placement via thoracotomy has the advantages of placement under direct vision and suturing the electrode in position. The disadvantages are that it requires major surgery and that fibrosis with ensuing loss of capture will occur, necessitating replacement.

Major Disadvantages Of This Simple Procedure

Placement in the lumen of the right ventricle via right jugular catheterization is a relatively simple procedure in experienced hands and precludes the fibrosis which

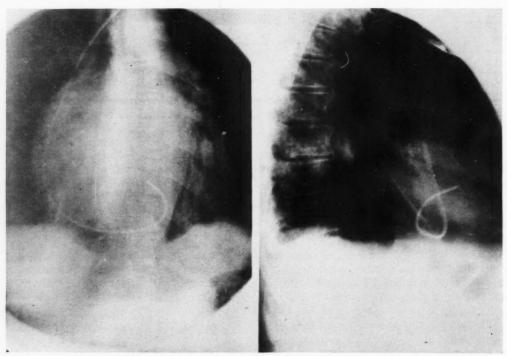


Figure No. 2 — Intracardiac electrode placed in the chamber of the right ventricle by insertion of a cardiac catheter through the right jugular vein.

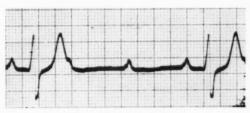




A - Before pacemaker



B — With pacemaker



C - After pacemaker

limits the duration of effectiveness with placement in the ventricular wall. The major disadvantage is that continuous anticoagulation with all of its inherent hazards is necessitated.

The method of application will obviously depend on the facilities at hand and the status of the patient.

Case Report

A 56 year old mechanic, was admitted to the Delaware Hospital February 16, 1960, for therapy of Stokes-Adams syndrome. He first showed a slow heart rate in September, 1959, and his electrocardiogram revealed first and second degree heart block. On several occasions he had syncopal attacks without warning. On January 4th he was hospitalized following two syncopal attacks. At this time the electrocardiogram revealed complete heart block which had persisted to date in spite of the

use of sympathomimetic amines and steroids.

Medical History

There was no known heart disease; specifically, there was no history of angina or rheumatic fever.

The patient was a healthy white man in no acute distress but frightened by syncopal attacks which were often accompanied by vomiting and loss of sphincter control. His pulse was irregular; the rate was 22 per minute. His blood pressure was 175/60. Auricular contractions were audible as was a bruit de canon. No murmurs or rubs were present. Otherwise, complete physical examination revealed no abnormalities.

Laboratory studies, including plasma chlorides, serum sodium, and serum potassium, were normal.

The electrocardiogram showed complete heart block with a ventricular rate of 20 per minute. (Fig 3-A) The patient was given intravenous molar lactate as well as isopropylarterenol, epinephrine and ephedrine with no response. He was then given cortisone, 200 mgm. daily, without effect. The external conventional pacemaker was tried but could not be tolerated because of chest wall shock and pain. Thyroid was added to the above program without benefit.

On February 26th the Atronic internal pacemaker was obtained and the intracardiac electrode was inserted* under local anesthesia into the right ventricular wall transthoracically through the specially designed needle described previously. The needle was passed in the fourth left intercostal space at the midclavicular line.

The patient's heart rate was controlled with the pacemaker at 50-60 per minute. On 2-28-60 capture was lost and the electrode was replaced in the myocardium. Subsequent ECGs showed second degree heart block with 3:1 A-V conduction and a ventricular rate of 30 per minute without the pacemaker. (Fig. 3-C) With the pacemaker in operation, the rate was controlled at 50-60 per minute. (Fig. 3-B)

^{*}Dr. Richard N. Taylor, Associate in Surgery.

DELAWARE MEDICAL JOURNAL

Over the ensuing weeks in the hospital, the patient returned to second degree block with varying 2:1 and 3:1 A-V conduction and a ventricular rate of 36-40 per minute.

The patient was discharged on March 19th with the intracardiac electrode in place and his family instructed in the use of the Atronic pacemaker.

The patient went four weeks after discharge without a Stokes-Adams attack. Following this he was off the pacemaker for periods of two to three days without syncope and his rhythm was second degree heart block with 2:1 A-V conduction and a ventricular rate of 40 per minute. The intracardiac electrode has now been removed with no syncope to date. In this case the intracardiac pacemaker maintained a cardiac rate and output sufficient to supply adequate cerebral blood flow until the patient's A-V conduction improved enough to maintain adequate blood flow to vital organs.

DISCUSSION

The treatment of the Stokes-Adams syndrome has been ineffective in our hands in the past in spite of a variety of therapeutic agents. While others have reported good results with sympathomimetic amines, molar sodium lactate, steroids, and the conventional external pacemaker, none has been uniformly effective.

Recently a small portable intracardiac pacemaker has been devised. The intracardiac electrode may be inserted into the myocardium transthoracically through a large needle; or may be placed into the chamber of the right ventricle via right jugular catheterization; or may be sewn into the ventricular wall via thoracotomy.

For long term use, insertion on a catheter into the right ventricular chamber is the most efficacious. One case to our knowledge has gone at least ten months with good capture with this method of insertion. However, this method requires continuous anticoagulation.

Bellet³ has reported four cases of Stokes-Adams syndrome in which the intracardiac pacemaker was used. In two of these patients the results were good. In the other two, permanent cerebral damages had occurred prior to the use of the intracardiac pacemaker, and the patients succumbed although successful cardiac stimulation was obtained in both instances. This stresses the importance of prompt initiation of therapy in Stokes-Adams syndrome.

SUMMARY

A case is presented of Stokes-Adams syndrome successfully treated with the intracardiac pacemaker. In this case the intracardiac electrode was inserted transthoracically via a 16 gauge needle under local anesthesia. There were no untoward effects from the procedure. Capture was maintained except for a short period when the electrode had come out of the myocardium and had to be reinserted. The patient's family was instructed in the operation of the pacemaker, and the patient was discharged, improved, to be followed by his family physician.

Conclusion

The indication for use of the intracardiac pacemaker in complete heart block is the presence of the Stokes-Adams syndrome in which drug therapy and external electrical stimulation have failed.

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PUNCH PLEURAL BIOPSY

• Pleural biopsy is commonly done under direct vision in the operating room and under "indirect vision" at the patient's bedside. In this country the Vim Silverman needle has been used extensively. The author presents the 'punch pleural biopsy' technique as yielding a more adequate specimen which carries with it no increased risk.

CHARLES A. R. SKOWRON, M.D.*

Pleural biopsy is valuable as an aid in the diagnosis of certain intrathoracic pathology in which pleural effusion is present.^{2,3} To have no positive diagnosis, but to prescribe for the patient along the suspected diagnostic impression has had unfortunate results. Much help has come from the use of the needle biopsy.^{3,4} The purpose here is to present a simple method of pleural biopsy in which the specimen yield is greater and more adequate than previous methods.

MATERIALS AND TECHNIQUES

Thoracentesis tray
Wide blade scalpel
Kerrison rongeur (Figure 1)

The patient is premedicated with a barbiturate. The biopsy site has previously been determined by clinical examination, x-ray, and fluoroscopy. The patient is comfortably adjusted in the sitting position, feet over the side of the bed resting on a stool or chair, and the arms permitted to support and balance the patient by resting on an over-bed table. The chest wall is prepared with Merthiolate and alcohol and 1% procaine anesthesia is used. A two inch #15 guage needle on a 2 cc. syringe is introduced into the pleural cavity over the upper margin of the rib, avoiding vessels and nerves by keeping away from the upper part of the interspace. Introduction of a needle is done to be sure that the biopsy will be taken from a site where free pleural fluid is present. With needle in place a

^{*}Director of tumor clinic at the Delaware Hospital, Wilmington.



KERRISON RONGEUR Figure 1

stab incision with a wide blade scalpel is made against the needle into the pleural space; no deeper. The incision should be about 3/8" long-only large enough to admit the Kerrison rongeur - keeping an air tight, water tight fit. The needle and scalpel are withdrawn. Immediately the rongeurs are inserted in a closed position felt to go past the upper edge of the rib just into the pleural space. The rongeur is permitted to open about one quarter inch and pressure is exerted with the rongeur in the direction of its biting lips. The rongeur is directed parallel to the rib and not toward the rib above. It is gently withdrawn until it is felt to engage the pleura. The rongeurs are closed, held in place for a few moments, and the specimen is then withdrawn. If desired, three or four specimens may be obtained.

The instrument is operated with one hand while the other is free to pinch the chest wall tissues together momentarily after removal of the specimen. Light pressure dressing is then applied.

Discussion

The specimens obtained for examination by the pathologist are much larger, being 4 or 5 mm. in diameter, and present less distortion and are more suitable for microscopic examination than the specimens obtained by a needle biopsy. The procedure is simple and is done easily at the patient's

bedside. Danger of lung puncture from the rongeur is almost nil because of its blunt tip, but caution must be exercised in creating the stab incision. One is guided here by the known length of the 15 guage needle and the fact that its tip is within the pleural space. This procedure is not recommended for a patient without pleural effusion or in the extremely emaciated patient whose intercostal spaces are depressed. In the first instance, damage may be done to underlying tissue. In the second one, there may be the possibility of introducing a pneumothorax because of the meager amount of tissue between skin and parietal pleura. The procedure is painless and of short duration, with minimal discomfort to the patient afterward. Pneumothorax has not been produced. To obtain no pleural specimen is almost unknown, whereas with the needle biopsy technique the percentage of yield of an adequate pleural biopsy is reported to be between 50 to 80%.

The only procedure for punch biopsy of the pleura found in the literature is that described by Abrams.¹ His instrument consists of concentric tubes and a stylet. It requires two free hands to maneuver, but can also be used to aspirate the fluid at the same time.

The Kerrison rongeur is easier to use, and the instrument is more readily available, for it can be used also by the orthopedic and neuro-surgeons in their field. Kerrison rongeurs have been used here because they are readily available. Other similar rongeurs may be used with equal ease.

SUMMARY

A procedure for pleural biopsy has been presented. The technique is easily done, the specimens more adequate for examination and the distress to the patient is minimal.

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Editorials

INTERNAL MEDICINE -

The delightful discussion of the past and future of Internal Medicine that appears as the lead article in this issue was not written for publication. Six months ago the director of a medical department sent it as a memorandum to all members of that department. Much confusion exists regarding the definition of an internist and internal medicine. It would be impossible for any article or memorandum to give the answers to these questions; in fact, Dr. Flinn actually adds another definition of an internist. He has, however, given excellent advice to young internists, which, if followed, will not only insure the future of Internal Medicine but will strengthen the position of the medical profession in the community.

CARDIAC SURGERY -

The June 25th issue of the J.A.M.A. contains a much needed and long awaited guest editorial entitled Factors to be Considered in Surgery for Closure of Ventricular Septal Defects. While long overdue, this message was worth waiting for when presented by someone of Dr. Helen Taussig's stature. Dr. Taussig states that despite the ever increasing number of congenital cardiac defects that are becoming amenable to surgery, surgery is not indicated in every instance. We must realize that some patients with congenital heart disease are capable of living a normal life; we must never underestimate the danger of open heart surgery. Certainly, in many instances, our technic is improving so rapidly that by waiting several years we may well get a better and safer operation. Dr. Taussig's editorial should be read by every practicing physician.

HYPNOSIS -

Should an operator with no knowledge of pathology be allowed to perform surgery? Should a physician with no knowledge of pathology prescribe drugs for the treatment of a pathological condition? Then why should a person with no knowledge of psychopathology be permitted to perform hypnosis? Meldman presents a case history in the May 28th J.A.M.A. in which hypnosis was used on a young man and resulted in suppression of his symptoms and their replacement by a much more serious set of problems. Hypnosis is a valuable but dangerous tool and its use should be restricted to physicians with a special knowledge of psychopathology.

CARDIAC PACEMAKER -

Elsewhere in this issue is a report of the first patient in Delaware to have the benefit of an internal cardiac pacemaker. Over the years many drugs have been recommended in the treatment of Stokes-Adams attacks. Recently isoproterenol hydrochloride and steroid therapy have been given some credit for success in treatment. For the past few years, occasional patients have been tided over a crisis by the use of the external cardiac pacemaker. As is true in so many conditions, the simplest remedy is sometimes the best and a forceful blow on the sternum of a patient in such an attack frequently is followed by the resumption of cardiac activity. Nevertheless in this age of instrumentations it is only fitting that progress be made along the lines of the establishment of cardiac rhythm and the use of a small transistorized pacemaker attached to the heart by internal electrodes is certainly progress. We congratulate the authors. Best wishes for continuing this work.

In Brief

Report On Oral Vaccine Following the release of reports on the use of the Sabin, or live virus, polio vaccine in the USSR during the past year, Surgeon General Leroy E. Burney stated that the U.S.P.H.S. will undertake an immediate and exhaustive analysis of the safety and effectiveness of this oral vaccine before licensing it for public use. In the meantime, Dr. Burney urged the continued use of the highly effective Salk vaccine in fighting polio.

Medical Testimony Upheld In an industrial accident case, tried in May of this year, the Delaware Supreme Court ruled that "Medical testimony may properly be the basis of the Board's decision notwithstanding the fact that the testimony of claimant and his witness was contradictory." In this case the decision of the Accident Board, in favor of the employer, was upheld by the Supreme Court.

VD Wave

The year 1960 threatens to develop the highest national syphilis incidence in 10 years, according to Chicago Public Health Service official, Clifford H. Cole, M.D. In addressing the Illinois Social Hygiene League, he warned the nation of a coming wave of syphlis attributed to the juvenile group who are attempting to assume the role of adults in respect to possessions and sex activity.

Research Retirement David Marine, M.D., was the recipient of the Kober Medal of the Association of American Physicians at their Annual Meeting in Atlantic City, May 4th. The 1960 gold medal, given for outstanding achievement in medicine, was awarded to Dr. Marine for his research on the physiology and pathology of the thyroid gland. Retired and living in Rehoboth Beach, Delaware, Dr. Marine has expanded his love of research to delving into Sussex County history and archeology.

Staff Of Life Expanded L-lysine added to a bread diet may enable the body to retain larger amounts of protein, according to experiments made in the DuPont Company's electrochemicals department. Dr. Harold Rice, a nutritionist with the company, reviewed a study made with Purdue University students, at a meeting of the American Institute of Nutrition.

Radiation Fear

The beneficial side of radiation was stressed by Robert W. Frelick, M.D., chief of the isotope laboratory, Memorial Hospital, and Dr. Arnold W. Clark, professor of biological sciences at the University of Delaware, in addressing a meeting of Atoms and Us at the Highlands Elementary School. Both men urged that individuals requiring x-rays leave the decision to the attending physician and not worry about ill effects which might result from radiation. Public instruction on radiation properly used will do much to dispel the fear induced by atomic "fall-out" publicity.

Golf Honors

The Second Golf Handicap Tournament for the championship of the New Castle County Medical Society was held in conjunction with the Annual Social Meeting at the Hercules Country Club on June 23, 1960. The top honors went to Doctors Haynes B. Cates, Frederick A. Bowdle, and John C. Pierson. Prizes were also won by Doctors Robert M. Marine, Major Wilson Gasper, and Paul A. Shaw.

Cancer Research Funds

An announcement was made by the Delaware Division of the American Cancer Society that funds are available for research in the State of Delaware. Information about applications may be had at their headquarters in the Academy of Medicine Building, 1925 Lovering Avenue, Wilmington 6, Delaware.

The Price Of Inflation

A \$26,030 income of today is no better than the \$10,000 income of 1939, says the National Industrial Conference Board. A married man with two children (the basis for all figures) making \$5,000 in 1939 would have \$4,941 to spend—\$59 being allotted to income and social security taxes. Twenty-one years later the same man now has to make \$12,307 a year in order to have the spending power of \$4,941 in 1939 dollars. Income and social security taxes for \$12,307 would be \$1,877—and the biggest bite, inflation, would cost \$5,489. No allowances were made in this survey for state, local or other federal taxes. The loss of purchasing power of the American dollar was based on changes in the consumer price index of the Bureau of Labor Statistics.

Personal Glimpses

Willard F. Preston, M.D., Wilmington, received an honorary degree at the commencement exercises of his undergraduate school, Mt. St. Mary's College, Emmitsburg, Maryland . . . George J. Boines, M.D. and James P. Walsh, M.D., presided at a seminar for physicians on the care of the aged held at St. Francis Hospital . . . Clarence J. Prickett, M.D., was reappointed for a three year term to the board of trustees of the Delaware State Hospital . . . George P. Rosemond, M.D., has been promoted to professor and co-chairman of the department of surgery at Temple University School of Medicine . . . Dr. M. A. Tarumianz headed the speakers at the annual Parents Day ceremony held at Stockley's Hospital for the Mentally Retarded; a bronze bust of Dr. Tarumianz was unveiled and placed in the lobby of the medical center . . . Gerald A. Beatty, M.D. was re-elected president of the Delaware Tuberculosis and Health Society (formerly the Anti-Tuberculosis Society) for the 9th year; Samuel G. Elbert, Jr., M.D. and Alfred R. Shands, Jr., M.D., were elected to the Executive Committee . . . Otakar J. Pollak, M.D., elected president of the Beebe Hospital staff; Ulo Ware, M.D., vice-president and A. L. Czebotari, secretary . . . Lemuel C. McGee, M.D., read a paper Medical Care in Industry at the 2nd Seminar on Occupational Health held at Colombia Medical School, Colombia, S.A.; Mrs. McGee, President of the Woman's Auxiliary to the Medical Society of Delaware, and their two daughters accompanied Dr. McGee on the trip to Medellin . . . Arnold H. Williams, M.D., was installed as president of the Laurel Rotary Club . . .

Delaware's delegate to the AMA reports on the proceedings of the 109th Annual Meeting, with emphasis on health care for the aged, pharmaceutical problems, relations with other health groups, and occupational health programs.

REPORT ON THE 1960 ANNUAL MEETING of the American Medical Association

H. THOMAS McGuire, M.D.

Nearly a hundred reports and resolutions occupied the delegates to the 109th Annual Meeting of the American Medical Association, held in Miami Beach, June 13-17. They included matters of policy which will affect medicine on the national and local levels for many years to come. The major issues involved health care for the aged, pharmaceutical problems, relations with other health groups, and occupational health programs.

Aged Care

As might have been expected, in view of the furor surrounding health care for the aged, this subject occupied a considerable part of the Delegates' time. Of great importance to a proper understanding of the AMA's position on this problem was a supplementary report of the Board of Trustees recapitulating the status of plans for the health care of the aged, and reviewing the AMA's efforts in this field. This report made clear the existence of the Committee on Geriatrics (later the Committee on Aging) as a part of the Council of Medical Service well before the adoption of the aged group as political capital by those seeking extenson of a national compulsory health insurance program.

Progressing to the charge that the medical profession has opposed dangerous legislation, but has failed to present a positive program of its own, the Board of Trustees reviewed the AMA program with the emphatic notation that allegations of negativism on the part of the profession have been untrue.

Positive Program

Briefly, the positive program embraces support of governmental participation in the purchase of health care for indigent persons; support of the FHA amendment providing for mortgage assistance for expansion of proprietary nursing homes; participation with other organizations in the development of home care programs and homemaker services; provision of leadership in promoting the expansion of health insurance plans and the development of new and more effective methods of prepayment: active support of efforts to eliminate the mandatory retirement at 65 and discriminatory employment practices against those over 45.

The Board of Trustees restated the Association's policy as one of supporting every assistance, including governmental assistance, for the sick who are in direct need of this kind of help. The Association has not and does not endorse governmental assistance for those sick who are able to prepay or otherwise pay their own health costs.

Summarizing this policy, the House of Delegates adopted the following statement as the official stand of the Association:

"Personal medical care is primarily the responsibility of the individual. When he is unable to provide this care for himself, the responsibility should pass to his family, the community, the county, the state, and only when all these fail, to the federal government, and then only in conjunction with other levels of government in the above order. The determination of medical needs should be made by a physician and the determination of eligibility should be made at the local level with local administration and The principle of freedom of control. choice should be preserved. The use of tax funds under the above conditions to pay for such care, whether through the purchase of health insurance or by direct payment, provided local option is assured, is inherent in this concept and is not inconsistent with previous actions of the House of Delegates of the American Medical Association."

In other actions on aging, the House authorized a national assembly to develop the specifics of health service and facilities for the aged, with a report by the AMA to the people.

Pharmaceutical Issues

In the pharmaceutical area the House made one statement of policy and took action to consider the charges made against the drug industry before a committee of the U.S. Senate.

As policy, the House agreed with the pharmacy profession that the filling of prescriptions by mail order is not in the best interest of the patient, except when the geographical isolation of the patient makes it necessary. The House pointed out that in the mail order process the direct relation between patient, physician and pharmacist is lost, and that this does not contribute to the public health or welfare.

Acting upon a resolution introduced from Delaware, the House directed the Board of Trustees to submit an appraisal of the current situation in the pharmaceutical industry to the House in June of 1961. The wording of the resolution, as introduced by me and amended by the Reference Committee, spells out the reasoning behind this request for an appraisal:

"WHEREAS, Current legislative investigations of the pharmaceutical industry have created doubts and questions in the public mind concerning the development, testing, approval, pricing, and marketing of drugs; and

WHEREAS, Certain proposals have been made which, if carried out, might impair the future of pharmaceutical research and development, thus retarding the progress of scientific therapy; and

WHEREAS, The services of the pharmaceutical industry are so vital to the public and to the medical profession that an objective study should be made; therefore be it

RESOLVED, That the Board of Trustees be directed to request the Council on Drugs and other appropriate Councils and Committees of the Association to study the pharmaceutical field and its relationship to medicine and the public, to correlate available material, and after consultation with the several branches of clinical medicine, clinical research, and medical education and other interested groups or agencies, submit an objective appraisal to the House of Delegates in June, 1961."

Allied Health Groups

The House received and approved the final report from the Committee to Study the Relationships of Medicine with Allied Health Professions and Services. The report covered the present situation of these relationships, and their future implications, and suggested principles for activating physician leadership in this area. The House recommended continuing AMA activity and approved the appointment of a committee of the Board of Trustees to carry on this work,

Specific approval for promoting cooperative efforts with the allied health professions

and services went to the following AMA activites:

- A conference with scientists in related fields to promote permanent cooperative activity.
- Conferences between national specialty societies and non-physician scientists specifically allied to the area of medical practice concerned.
- Conferences with professional and technical assistants concerning education, recruitment, and coordination of activities.
- Reciprocal exchange of information between physicians and other scientists through joint meetings and publications.
- 5. Liaison between representatives of the AMA and other professional and technical groups.

Occupational Health Programs

The House expanded somewhat the statement on "Scope, Objectives and Functions of Occupational Health Programs" originally adopted in June, 1957. The new statement places greater emphasis on the preventative and health maintenance concepts of occupational health programming, and makes more positive organized medicine's obligation to improve occupational health services by part-time physicians in small industries. As corrolaries, this statement includes guidance on the proper use of immunization procedures for employees and stresses the need for teamwork with lay industrial hygienists in suiting the occupational health program to the specific employee group that it serves.

The new statement also places increased emphasis on rehabilitation of the occupationally ill and injured, which complements a projected study by the Council on Occupational Health of the employment of the physically handicapped.

Highlights

In actions affecting hospital staffs, the House approved contingent appointments of not more than 6 months for foreign medical school graduates who have been accepted for the September, 1960 screening examination, and asked the Board of Trustees to initiate a study of content and methods of preparation of hospital records.

In actions affecting members as individuals, the House directed the Board to develop group annuity and group disability insurance programs for Association members, and reaffirmed its opposition to compulsory inclusion of physicians under the Social Security Act; urged reform of the federal tax structure to return to the states and their subdivisions sources of revenue; decided against establishing a home for aged and retired physicians; and urged individual members of the AMA to take greater interest and more active part in public affairs on all levels.

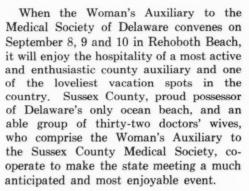
Dr. Louis M. Orr, retiring AMA president, urged medical societies to "adopt" rural villages, cities, etc., in undeveloped parts of the world and to send them medical and hospital supplies. Dr. Orr specifically commended the Junior Chamber of Commerce of Wilmington for its efforts in supplying medicines to a leper colony in Thailand.

Dr. E. Vincent Askey, incoming president, declared in his inaugural address that the decade to come will present medicine with its greatest challenge, that of proving the effectiveness of practice in a free society. In a later address, Dr. Askey urged intensive, accelerated effort in medical education, health insurance, third-party relationships, mental health, and AMA membership relations.

Dr. Leonard W. Larson of Bismark, North Dakota, former Chairman of the Board of Trustees, was unanimously elected president-elect. Dr. Larson will become president at the June, 1961, meeting in New York City. Dr. H. Thomas McGuire of Delaware was nominated for election to the Council on Medical Service but withdrew in favor of Dr. Russell B. Roth, an incumbent re-elected to the Council.

Auxiliary Affairs

Left to hight: Mrs. James B. Homan of Milford, publicity chairman; Mrs. Leslie M. Dobson, president; Mrs. Aubrey C. Smoot, Jr., treasurer, and Mrs. James Beebe, Jr., vice president.



Since our President-elect, Mrs. J. Leland Fox of Seaford, will be installed at the Convention as president of the State Auxiliary for the 1960-61 year, there is an added note of pride in this year's proceedings. This is the second time that Mrs. Fox has been gracious enough to serve as president of the State Auxiliary and she has an enviable record of participation in all phases of Auxiliary affairs.

At the County level, the Auxiliary operates as an active service and social organization under the efficient leadership of Mrs. Leslie M. Dobson of Milford, president. They meet at the homes of their members, with meetings planned to coincide with their husbands' monthly meetings on the second Thursday of the month. Serving with Mrs. Dobson are Mrs. James Beebe,



Jr., of Lewes, vice president; Mrs. Carleton C. Fooks of Milford, secretary; and Mrs. Aubrey C. Smoot, Jr., of Georgetown, treasurer.

Their principal service project has been aid for the Hospital for the Mentally Retarded at Stockley. They have sent personalized gifts and contributions to the patients on all appropriate holidays and occasions and have a deep interest in supplying what small pleasures they can to the patients.

In addition to support of local charities and schools, the Auxiliary is untiring in its effort to contribute to the American Medical Education Foundation. In 1958-59, they were able to contribute twice as much as they had pledged through the sale of Christmas cards. They hope to maintain this same high standard in 1959-60 through the sale of Delaware seals and donations.

In addition to Mrs. Fox, the Sussex County Auxiliary is proud to note three more active participants on the Executive Board of the State Auxiliary. Mrs. Robert F. Lewis of Seaford who has worked untiringly on the county scholarship committee, is also state treasurer. Mrs. Laurance L. Fitchett of Milford is state chairman of Mental Health, and Mrs. Carleton C. Fooks is state chairman of Civil Defense.

Books

Recent Accessions to the Library of the Delaware Academy of Medicine

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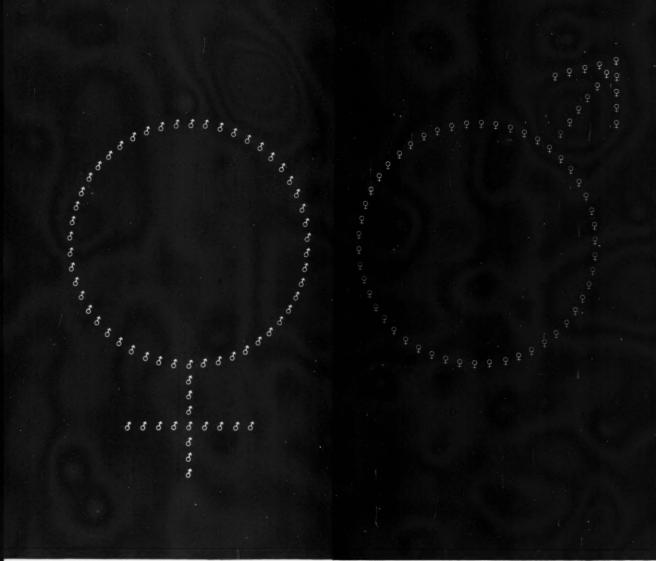
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Marmell, M., and Prigot, A.: Tetracycline phosphate complex in the treatment of acute gonococcal urethritis in men. Antibiotic Med. & Clin. Ther, 6:108 (Feb.) 1959.



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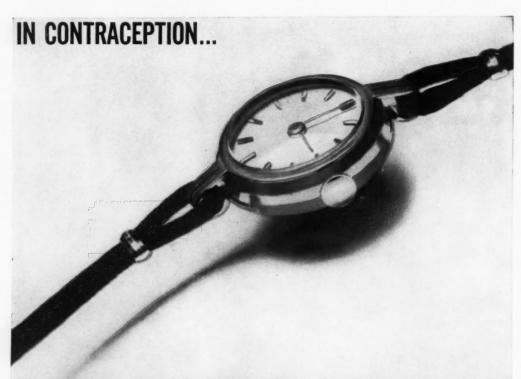
References: 1, Fabricant, N. D.; E. E. N. T. Monthly 37:460 (July) 1958. 2. Lhotka, F. M.; Illinois M. J. 112:259 (Dec.) 1957. 3. Farmer, D. F.; Clin, Med. 5:1183 (Sept.) 1958. 4. Fuchs, M.; Bodi, T.; Mallen, S. R.; Hernando, L., and Moyer, J. H.; Antibiotic Med. & Clin, Ther. 7:37 (Jan.) 1960. 5. Halpern, S. R., and Rabinowitz, H.; Ann. Allergy 18:36 (Jan.) 1960.

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*Berberian, D. A., and Slighter, R. G.: J.A.M.A. 168:2257 (Dec. 27) 1958.

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. . Atarax appeared to reduce anxiety and restlessness, improve sleep pat-terns and make the child more amenable to the development of new patterns of behavior..." Freedman, A. M.: Pediat. Clin. North America 5:573 (Aug.) 1958.

. seems to be the agent of choice in patients suffering from removal dis-orientation, confusion, conversion hys-teria and other psychoneurotic condi-tions occurring in old age." Smigel, J. O., et al.: J. Am. Geriatrics Soc. 7:61 (Jan.) 1959.

"All [asthmatic] patients reported greater calmness and were able to rest and sleep better...and led a more normal life....ln. chronic and acute urticaria, however, hydroxyzine was effective as the sole medicament." Santos, I. M., and Unger, L.: Presented at 14th Annual Congress, American College of Allergists, Atlantic City, New Jersey, April 23-25, 1958.

"... especially well-suited for ambulatory neurotics who must work, drive a car, or operate machinery." Ayd, F. J., Jr.: New York J. Med. 57:1742 (May 15) 1957.

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Bayart, J.: Acta paediat. belg. 10:164, 1956. Ayd, F. J., Jr.: California Med. 87:75 (Aug.) 1957. Nathan, L. A., and Andelman, M. B.: Illinois M. J. 112:171 (Oct.) 1957.

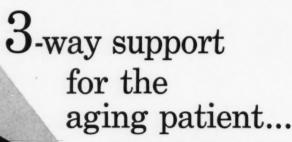
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Garber, R. C., Jr.: J. Florida M. A. 45:549 (Nov.) 1958. Menger, H. C.: New York J. Med. 58:1684' (May 15) 1958. Farah, L.: Inter-nat. Rec. Med. 169:379 (June) 1956.

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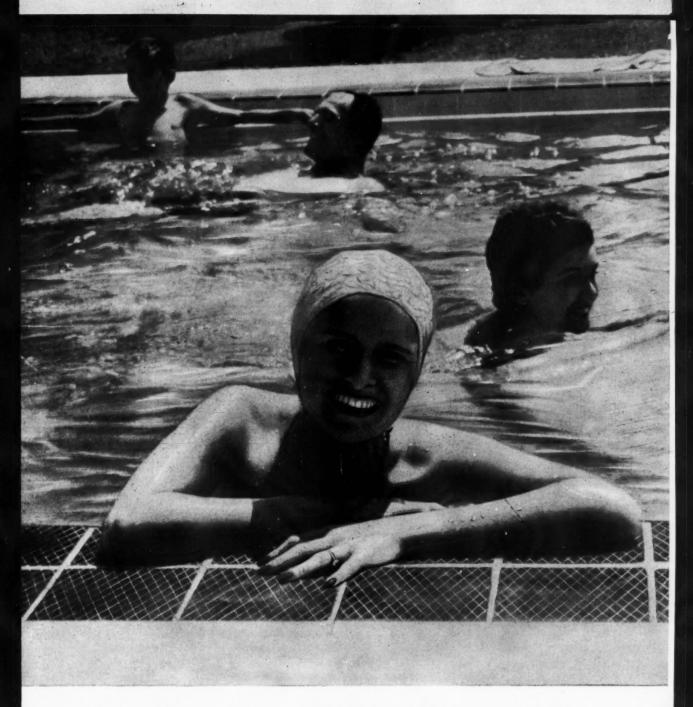
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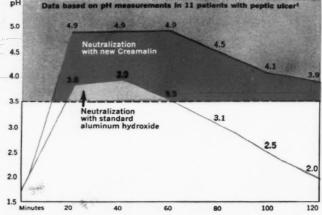
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1. Data in the files of the Department of Medical Research, Winthrop Laboratories. 2. Hinkel, E. T., Jr.; Fisher, M. P., and Tainter, M. L.: J. Am. Pharm. A. (Scient. Ed.) 48:384, July, 1959.

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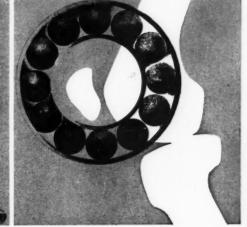
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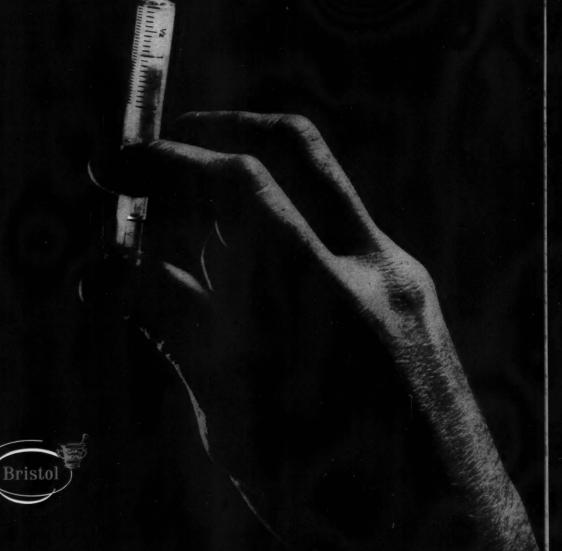
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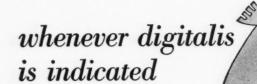
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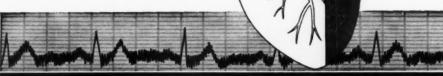
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REFERENCES: I. Yow, E. M.: Practitioner 182:759, 1959. 2. Yow, M. D., and Womack, G. K.: Ann. N. Y. Acad. Sci. 76:363, 1958. 3. Bunn, P. A., Baltch, A., and Krajnyak, O.: Ibid. 76:109, 1958. 4. Council on Druga, J.A.M.A. 172:699, 1960.

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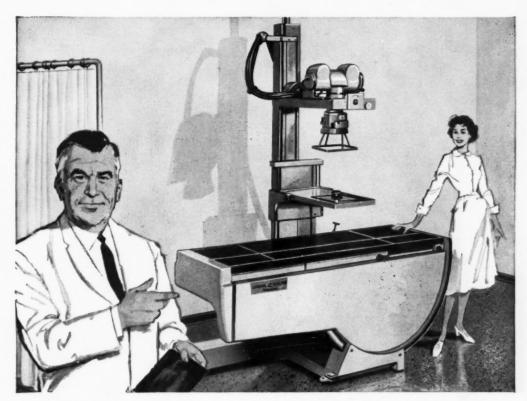
Lown, B., and Levine, S. A.: Current Concepts in Digitalis Therapy, Boston, Little, Brown & Company, 1954, p. 23, par. 2.

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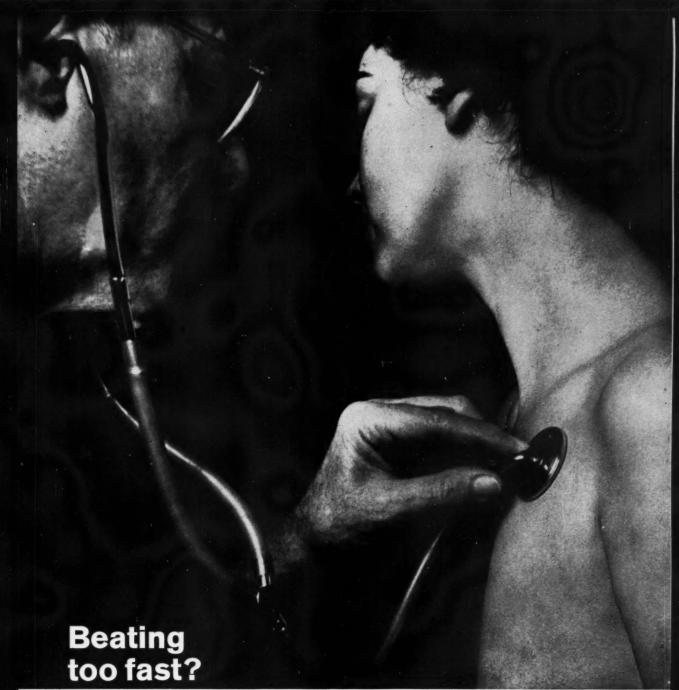
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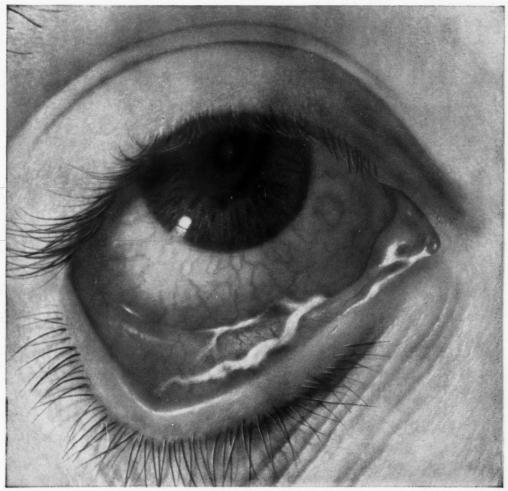
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 Gordon, D.M.: Am. J. Ophth. 46:740, November 1958.

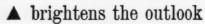
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1. Goddard, E.S.: in Trifluoperazine, Further Clinical and Laboratory Studies, Philadelphia, Lea & Febiger, 1959.

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